NMCP COVID-19 Report: Thursday, 09 April 2020

Prepared by: Tracy Shields, MSIS, AHIP <tracy.c.shields2.civ@mail.mil>
Reference Medical Librarian; Naval Medical Center Portsmouth, Library Services

Disclaimer: I am not a medical professional.

Statistics (as of Thursday, 09 April 2020 at 1500)

Global total confirmed cases: 1,536,979	
United States	*Virginia*
Estimated peak resource use: 11 April 2020 (projection from UW IHME) JHU CSSE Confirmed Cases: 451,491 NY: 160,038 NJ: 51,027 MI: 20,346 Total deaths: 15,774 NY: 7,067 NJ: 1,504 MI: 959 Total recovered: 24,790 Dept VA Positive Veteran Cases: 3,504	Estimated peak resource use: 20 April 2020 (projection from UW IHME) VA DOH Total cases: 4,042 Chesapeake: 101 Hampton: 53 Newport News: 64 Norfolk: 84 Portsmouth: 44 Suffolk: 31 Virginia Beach: 219 Total hospitalizations: 685 Total deaths: 109 Dept VA Hampton VAMC: 16 inpatient, 18 outpatient

Looking Ahead

Planned for the Tuesday, 14 April 2020 report are summaries on palliative care (support for patient and families, training healthcare workers) and air transport for patients with COVID-19.

Evidence Summary: Testing

Testing Types

Two types of tests are done to detect active infection of SARS-CoV-2 and support diagnosis of COVID-19: molecular and antibody tests. As of this writing, the FDA has approved 30 different test kits and commercial laboratories for COVID-19, with each test having specific parameters on accuracy, sensitivity, and specificity (FDA EUAs). There are efforts to collate commercially available tests and those in development for COVID-19 diagnosis (360Dx; FindDx).

Point-of-care (POC) testing

Most testing is molecular-based and performed in a laboratory setting, but POC testing will be necessary, especially in operational environments. Oxford's Centre for Evidence-Based Medicine posted a summary on COVID-19 POC testing on 07 April 2020. They note:

> "Moving diagnostic testing for COVID-19 from laboratory settings to the point of care is potentially transformative in the rate and quantity of testing that could be performed. Eleven diagnostic tests that are potentially suitable for testing for COVID-19 at the point-of-care are described: six molecular tests, and five antibody-based tests. Some devices show high diagnostic accuracy during controlled testing, but performance data from clinical settings, and a clear understanding of the optimal population and role for these tests in the care pathway, are currently lacking." (CEBM)

Molecular Testing

The reference test involves real time reverse transcriptase polymerase chain reaction (RT-PCR) assay using typed coronaviruses from biobanks and other sources (Euro Surveill). CEBM's summary on testing notes that misclassification errors can happen, and that "[f]ailure to amplify can be interpreted as a negative result, but could also be attributable to poor quality of the clinical sample or to early disease status" (CEBM). Molecular point-of-care tests work in the same way but automate steps to make operation possible nearer to patients and shorten test time.

The sensitivity of RT-PCR can vary depending on the laboratory. For example, documentation from LabCorp notes the limit of detection (LoD) with SARS-CoV-2/COVID-19 RT-PCR test is 6.25 genome copies(cp)/mcL; specificity testing found a variety of other organisms (e.g., adenovirus, parainfluenza, MERS, etc.) were negative, but there was some cross-reactivity with SARS (LabCorp).

Serological Testing

Serological tests detect the presence of antibodies (immunoglobulins M and G [IgM and IgG]) to coronavirus in whole blood, plasma, or serum samples, often using enzyme-linked immunosorbent assays (ELISA) (J Med Virol). These tests may not reliable if the body has not yet started making antibodies (typically 5-10 days post-infection).

A preprint article (i.e., not yet peer-reviewed) describes antigen testing for SARS-CoV-2 (bioRxiv*) but at this time there is no commercially available antigen tests for COVID-19.

Seroconversion

There are limited data at this time on seroconversion. In a study of 173 patients SARS-CoV-2 infection, the seroconversion rate for total antibodies, IgM and IgG was 93.1%, 82.7% and 64.7%, respectively, with median seroconversion times of 11 days, 12 days, and 14 days, respectively (Clin Infect Dis). One early release article detailing the virologic assessment of 9 hospitalized patients noted seroconversion (detected by IgG and IgM immunofluorescence) occurred in 50% of patients by day 7, and in all by day 14 (Nature). One article notes seroconversion for IgM antibodies occurs a few days earlier than IgG (BMC Cell & Bioscience). A preprint article describes a method of testing for seroconversion as early as 3 day after symptom onset (medRxiv*).

* bioRxiv and medRxiv are preprint servers: "[T]hese are preliminary reports that have not been peer-reviewed. They should not be regarded as conclusive, guide clinical practice/health-related behavior, or be reported in news media as established information."

See also: CEBM summary on comparison of oropharyngeal and nasopharyngeal swabs for laboratory diagnosis given in the 31 March 2020 NMCP COVID-19 Report.

Recent Literature

Radiology: The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society (07 April 2020)

> Intended to offer guidance to physicians on best uses of imaging for COVID-19 patients. The authors note that evidence is scant and their advice will likely be refined as the pandemic progresses. The essentials:
>
> > "Imaging is not indicated in patients with suspected COVID-19 and mild clinical features unless they are at risk for disease progression."
> >
> > "Imaging is indicated in a patient with COVID-19 and worsening respiratory status."
> >
> > "In a resource-constrained environment, imaging is indicated for medical triage of patients with suspected COVID-19 who present with moderate-severe clinical features and a high pre-test probability of disease."
>
> The article presents different scenarios of patients and environments that may be of value in decision making.

JAMA: A Bold Response to the COVID-19 Pandemic: Medical Students, National Service, and Public Health (08 April 2020)

> Editorial that discusses the impact of this pandemic on medical education, calling on the U.S. to suspend the first year of medical school for 1 year and have the students do a national service program for public health. Medical students could support public health systems, aid in testing, staff call centers, and become temporary case workers. The editors discuss how to handle the disruptions downstream in medical education and physician pipeline, with ideas on how to adjust to the changing medical workforce.

Of note, the New England Journal of Medicine has a similar call to action:

NEJM: Ensuring and Sustaining a Pandemic Workforce (08 April 2020)

> This perspective focuses more on third and fourth year medical students, and changes to education programs to train students in essential, immediately needed skills. These programs would be tied into surge planning and support the healthcare workforce in other ways. The authors also look at broader uses of established healthcare personnel like dentists, optometrists, and nonclinical positions.

JAMA: Understanding and Addressing Sources of Anxiety Among Health Care Professionals During the COVID-19 Pandemic (07 April 2020)

> This viewpoint outlines considerations leadership should have for their workforce during COVID-19 pandemic. They point out 8 sources of anxiety that arose from discussion with healthcare workers:
>
> > "(1) access to appropriate personal protective equipment, (2) being exposed to COVID-19 at work and taking the infection home to their family, (3) not having rapid access to testing if they develop COVID-19 symptoms and concomitant fear of propagating infection at work, (4) uncertainty that their organization will support/take care of their personal and family needs if they develop infection, (5) access to childcare during increased work hours and school closures, (6) support for other personal and family needs as work hours and demands increase (food, hydration, lodging, transportation), (7) being able to provide competent medical care if deployed to a new area (eg, non-ICU nurses having to function as ICU nurses), and (8) lack of access to up-to-date information and communication."
>
> The authors state that type of requests from providers to their organization during can be broken down as: "hear me"; "protect me"; "prepare me"; "support me"; and "care for me". Also: "A final overarching request of health care workers—even if only implicitly recognized—is "honor me.""

In Brief

Ventilators & Resource Scarcity

In anticipation of resource scarcity, Northwell Health system has released details on converting BiPAP machines for use as mechanical ventilators (Northwell [links to pdf at Dropbox]).

There is some discussion around overuse of invasive mechanical ventilation in a subset of COVID-19 patients, with arguments for more nuanced approaches to ventilator use possibly alleviating resource demands (STATnews).

With potential ventilator demands exceeding supply, there are increasing ethical concerns that vulnerable populations, including disabled people, may be at risk, and decision makers need to be aware of potential biases (WaPo; WaPo). Some hospital systems have released guidelines directing how to manage limited supply of ventilators (Politico). Relatedly, the HHS Office for Civil Rights and Action has published guidelines specific to COVID-19 (HHS).

Vaccines

There are calls to produce COVID-19 vaccines before they are known to work (STATnews). One company has started phase 1 clinical testing in healthy volunteers (Inovio).

Hospital Experiences

A recent survey of hospitals by the Department of Health and Human Services Office of Inspector General found hospitals face substantial challenges in maintaining and expanding care to patients, have widespread shortages of PPE, and problems maintaining adequate staffing levels (HHS).

References

Statistics

Dept VA: U.S. Department of Veterans Affairs. Public Health: Novel Coronavirus Disease (COVID-19). Link: https://www.publichealth.va.gov/n-coronavirus/

JHU CSSE: Johns Hopkins Center for Systems Science and Engineering. Coronavirus COVID-19 Global Cases. Link: https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html

UW: University of Washington, Institute for Health Metrics and Evaluation. COVID-19 projections assuming full social distancing through May 2020 (01 April 2020). Link: https://covid19.healthdata.org/

VA DOH: Virginia Department of Health. COVID-19 in Virginia, updated daily. Link: http://www.vdh.virginia.gov/coronavirus/

Evidence Summary

360Dx: Coronavirus Test Tracker: Commercially Available COVID-19 Diagnostic Tests. Link: https://www.360dx.com/coronavirus-test-tracker-launched-covid-19-tests

bioRxiv: Khan S, Nakajima R, Jain A, et al. Analysis of Serologic Cross-Reactivity Between Common Human Coronaviruses and SARS-CoV-2 Using Coronavirus Antigen Microarray. bioRxiv 2020.03.24.006544; doi: https://doi.org/10.1101/2020.03.24.006544. Link: https://www.biorxiv.org/content/10.1101/2020.03.24.006544v1.full

BMC Cell & Bioscience: Yuen KS, Ye ZW, Fung SY, Chan CP, Jin DY. SARS-CoV-2 and COVID-19: The most important research questions. Cell Biosci. 2020 Mar 16;10:40. doi: 10.1186/s13578-020-00404-4. eCollection 2020. PubMed PMID: 32190290; PubMed Central PMCID: PMC7074995. Link: https://cellandbioscience.biomedcentral.com/articles/10.1186/s13578-020-00404-4

CEBM: University of Oxford Centre for Evidence-Based Medicine. Molecular and antibody point-of-care tests to support the screening, diagnosis and monitoring of COVID-19 (07 April 2020). Link: https://www.cebm.net/covid-19/molecular-and-antibody-point-of-care-tests-to-support-the-screening-diagnosis-and-monitoring-of-covid-19/

Clin Infect Dis: Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, Wang X, Yuan J, Li T, Li J, Qian S, Hong C, Wang F, Liu Y, Wang Z, He Q, Li Z, He B, Zhang T, Fu Y, Ge S, Liu L, Zhang J, Xia N, Zhang Z. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis. 2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa344. [Epub ahead of print] PubMed PMID: 32221519. Link: https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa344/5812996

Euro Surveill: Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DGJC, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MPG, Drosten C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020 Jan;25(3). doi: 10.2807/1560-7917.ES.2020.25.3.2000045. PubMed PMID: 31992387; PubMed Central PMCID: PMC6988269. Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6988269/

FDA EUAs: U.S. Food & Drug Administration Emergency Use Authorizations (07 April 2020). Link: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

FindDx: SARS-CoV-2 Diagnostic Pipeline. Link: https://www.finddx.org/covid-19/pipeline/

J Med Virol: Xiao SY, Wu Y, Liu H. Evolving status of the 2019 novel coronavirus infection: Proposal of conventional serologic assays for disease diagnosis and infection monitoring. J Med

Virol. 2020 May;92(5):464-467. doi: 10.1002/jmv.25702. Epub 2020 Feb 17. PubMed PMID: 32031264. Link: https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25702

LabCorp: Laboratory Corporation Of America. Accelerated Emergency Use Authorization (EUA) Summary COVID-19 RT-PCR Test (accessed 09 April 2020). Link: https://www.fda.gov/media/136151/download

medRxiv: Amanat F, Nguyen T, Chromikova V, et al. A serological assay to detect SARS-CoV-2 seroconversion in humans. medRxiv 2020.03.17.20037713; doi: https://doi.org/10.1101/2020.03.17.20037713 Link: https://www.medrxiv.org/content/10.1101/2020.03.17.20037713v1.full.pdf

Nature: Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, Niemeyer D, Jones TC, Vollmar P, Rothe C, Hoelscher M, Bleicker T, Brünink S, Schneider J, Ehmann R, Zwirglmaier K, Drosten C, Wendtner C. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x. [Epub ahead of print] PubMed PMID: 32235945. Link: https://www.nature.com/articles/s41586-020-2196-x_reference.pdf

Recent Literature

JAMA: Bauchner H, Sharfstein J. A Bold Response to the COVID-19 Pandemic: Medical Students, National Service, and Public Health. JAMA. Published online April 08, 2020. doi:10.1001/jama.2020.6166 Link: https://jamanetwork.com/journals/jama/fullarticle/2764427

JAMA: Shanafelt T, Ripp J, Trockel M. Understanding and Addressing Sources of Anxiety Among Health Care Professionals During the COVID-19 Pandemic. JAMA. 2020 Apr 7. doi: 10.1001/jama.2020.5893. [Epub ahead of print] PubMed PMID: 32259193. Link: https://jamanetwork.com/journals/jama/fullarticle/2764380

NEJM: Fraher EP, Pittman P, Frogner BK, Spetz J, Moore J, Beck AJ, Armstrong D, Buerhaus PI. Ensuring and Sustaining a Pandemic Workforce. N Engl J Med. 2020 Apr 8. doi: 10.1056/NEJMp2006376. [Epub ahead of print] PubMed PMID: 32268021. Link: https://www.nejm.org/doi/full/10.1056/NEJMp2006376

Radiology: Rubin GD, Haramati LB, Kanne JP, Schluger NW, Yim JJ, Anderson DJ, Altes T, Desai SR, Goo JM, Inoue Y, Luo F, Prokop M, Richeldi L, Tomiyama N, Leung AN, Ryerson CJ, Sverzellati N, Raoof S, Volpi A, Martin IBK, Kong C, Bush A, Goldin J, Humbert M, Kauczor HU, Mazzone PJ, Remy-Jardin M, Schaefer-Prokop CM, Wells AU. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. Radiology. 2020 Apr 7:201365. doi: 10.1148/radiol.2020201365. [Epub ahead of print] PubMed PMID: 32255413. Link: https://pubs.rsna.org/doi/10.1148/radiol.2020201365

In Brief

HHS: Department of Health and Human Services, Office of Inspector General. Hospital Experiences Responding to the COVID-19 Pandemic: Results of a National Pulse Survey March 23-27, 2020 (03 April 2020). Link: https://oig.hhs.gov/oei/reports/oei-06-20-00300.pdf

HHS: Department of Health and Human Services, Office for Civil Rights and Action. BULLETIN: Civil Rights, HIPAA, and the Coronavirus Disease 2019 (COVID-19) (28 March 2020). Link: https://www.hhs.gov/sites/default/files/ocr-bulletin-3-28-20.pdf

Inovio: Press release. INOVIO Initiates Phase 1 Clinical Trial Of Its COVID-19 Vaccine and Plans First Dose Today (06 April 2020). Link: http://ir.inovio.com/news-and-media/news/press-release-details/2020/INOVIO-Initiates-Phase-1-Clinical-Trial-Of-Its-COVID-19-Vaccine-and-Plans-First-Dose-Today/default.aspx

Northwell: Link to document on Dropbox: https://www.dropbox.com/sh/6x52zmvxl5expjd/AAAa6-XoOZGUleVS4S7fKGIia?dl=0&fbclid=IwAR28Z160ccpOTc1WLYoxCgdi-Ikly_x0prg5Mny1E03fKZIMvp3AHFyxNUs

Politico: Amanda Eisenberg and Sally Goldenberg. Northwell memo calls for rationing ventilators to 'patients most likely to benefit' (03 April 2020). Link: https://www.politico.com/states/new-york/albany/story/2020/04/03/northwell-memo-calls-for-rationing-ventilators-to-patients-most-likely-to-benefit-1271711

STATnews: Sharon Begley. With ventilators running out, doctors say the machines are overused for Covid-19 (08 April 2020). Link: https://www.statnews.com/2020/04/08/doctors-say-ventilators-overused-for-covid-19/

STATnews: Helen Branswell. A $30 billion gamble: Pandemic expert calls for making Covid-19 vaccines before we know they work (07 April 2020). Link: https://www.statnews.com/2020/04/07/pandemic-expert-calls-for-making-coronavirus-vaccines-before-we-know-they-work/

WaPo: Washington Post. Neil Romano and Samuel Bagenstos. Don't deny ventilators to disabled patients (06 April 2020). Link: https://www.washingtonpost.com/outlook/2020/04/06/coronavirus-ventilators-disabled-people/

WaPo: Washington Post. Ariana Eunjung Cha and Laurie McGinley. Who gets a shot at life if hospitals run short of ventilators? (07 April 2020). Link: https://www.washingtonpost.com/health/2020/04/07/ventilators-rationing-coronavirus-hospitals/